

## REMARKS

Applicants thank the Examiner for recognizing that the claimed PRO335 antibody, as a composition of matter, is enabled based on the disclosure in the instant specification and knowledge available in the art.

However, the Examiner's Comment states that "The lack of enablement rejection of the claims under 35 U.S.C 112, first paragraph, made in the last Office Action (mailed on 2/20/08) was based on if the claimed invention is to be used for therapeutic enhancement of the immune response, the results of Example 74 (MLR assay) in the specification are not sufficient to support the enablement of the claims since there is no indication of the statistical significance of the results, and no autologous controls; no correlation is provided to any particular *in vivo* function; there is no guidance to indicate that PRO335 could be used to any therapeutic effect for the treatment of diseases such as cancer or HIV."

Applicants reiterate and maintain the position, as stated in their Amendment and Response, filed on August 19, 2008, that the positive result for PRO335 in the MLR assay demonstrates that PRO335 is active as a stimulator of the proliferation of stimulated T-lymphocytes. As discussed previously, the MLR assay was routinely used in the art to identify immunostimulants or immunosuppressors, and additionally, were found to have *in vivo* utility, in the treatment of various diseases and conditions. Further, the importance of immunostimulants in the treatment of cancer or in enhancing the effectiveness of previously identified treatments for cancer, including tumor-specific antibodies were well known in the art at the time of filing of the instant application, as discussed in several references made of record. For instance, costimulation of T cells inducing tumor regression and an antitumor response, both *in vitro* and *in vivo* was known (for e.g., Steinman *et al.* -submitted as Exhibit B with the Response filed August 30, 2004). Thus, one skilled in the art would know that immunostimulating compounds like IL-12 or PRO335 of this invention, could be useful in immunoadjuvant therapies, for the treatment of tumors (cancer) and could be administered either alone or together with other agents to stimulate T cell proliferation/ activation (immune function). Alternatively, based on disclosures in the patent application coupled with information known in the art, one skilled in the art would know that antagonistic antibodies (immunosuppressors), are useful for instance, in treating diseases like autoimmune or graft vs. host disease).

In further support of the utility of the MLR assay, Applicants have submitted (with their Response filed August 30, 2004) the Declaration of Sherman Fong, Ph.D. As Dr. Fong emphasizes, immunostimulants are important and highly desirable in the treatment of cancer and in enhancing the effectiveness of previously identified treatments for cancer. He further points out that costimulation of T cells can induce tumor regression and an antitumor response, both *in vitro* and *in vivo*.

Therefore, one skilled in the art would know that immunostimulating compounds like PRO335 of this invention, could be used in immunoadjuvant therapy (with tumor-specific antibodies) for the treatment of tumors (cancer) and could be administered alone or together with other agents to stimulate T cell proliferation/ activation (immune function).

#### **Change in Inventorship**

Having reviewed the allowed claims, Applicants have found that as a result of claim amendments made during prosecution, fewer than all of the currently named inventors are the actual inventors of the invention being claimed in the present application. Accordingly, please **delete** the names of the following inventors, who have not made an inventive contribution to the currently claimed subject matter:

<b>Ashkenazi, Avi</b>	<b>Botstein, David</b>
<b>Desnoyers, Luc</b>	<b>Eaton, Dan L.</b>
<b>Ferrara, Napolene</b>	<b>Filvaroff, Ellen</b>
<b>Fong, Sherman</b>	<b>Gao, Wei-Qiang</b>
<b>Gerber, Hanspeter</b>	<b>Gerritsen, Mary E.</b>
<b>Grimaldi, Christopher J.</b>	<b>Hillan, Kenneth J.</b>
<b>Kljavin, Ivar J.</b>	<b>Mather, Jennie P.</b>
<b>Pan, James</b>	<b>Paoni, Nicholas F.</b>
<b>Roy, Margaret A.</b>	<b>Stewart, Timothy A.</b>
<b>P. Miekey Williams</b>	

Upon entering the present amendment, **Audrey Goddard, Paul J. Godowski, Austin L. Gurney, Daniel Tumas and William I. Wood** remain named inventors in this case.

Please charge the fee of **\$130.00** and/or any fees that might become applicable, including any fees for extension of time, or credit overpayment to Deposit Account No. **50-4634**, referencing Attorney's Docket No. **GNE-1618 P2C47**.

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: April 14, 2009

  
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